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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/150,813	09/11/98	GRAINGER D	295.027US1

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EXAMINER	
MURPHY, J	

ART UNIT	PAPER NUMBER
1646	22

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/150,813	Applicant(s) GRAINGER ET AL.	
	Examiner Joseph F Murphy	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 June 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17,20,21,24-28,31-35,40-45,48-50 and 52-62* is/are pending in the application.

4a) Of the above claim(s) *21,24-28,31-33,35,45 and 48-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17, 20, 22, 34, 41-44, 52-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 19 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Formal Matters

Claims 55-56 were amended in Paper No. 21, 6/9/2001. Claims 17, 20-21, 24-28, 31-35, 40-45, 48-50, 52-62 are pending. Claims 21, 24-28, 31-33, 35, 45, 48-50 stand withdrawn from consideration pursuant to 37 CFR 1.142(b). Claims 17, 20, 22, 34, 41-44 and 52-62 are under consideration.

The text of those sections of Title 35, U. S. Code not included in this action can be found in a prior Office Action.

Response to Arguments

The rejection of claims 17 and 20 under 35 USC § 112, second paragraph has been withdrawn based on Applicant's argument citing the definition of "indication" in Stedman's Medical Dictionary.

The rejection of claims 17, 20, 22, 34, 41-44 and 52-62 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention has been withdrawn based on Applicant's arguments.

Claim Rejections - 35 USC § 112 first paragraph

Claims 17, 20, 22, 34, 41-44, 52-62 stand rejected under 35 U.S.C. 112, first paragraph, for reasons of record set forth in Paper No. 16, 11/29/2000, because the specification, while being enabling for a method of preventing dermal inflammation or asthma using CRD-$Leu_4Ile_{11}Cys_{13}$peptide 3(3-12)[MCP-1], it does not reasonably provide enablement for a method of preventing dermal inflammation or asthma using peptides of a peptide of a chemokine, variants thereof or derivatives thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In the previous Office Action, it was stated that claims 17, 20, 22 and 34 are overly broad in the recitation of "a peptide of a chemokine, a variant thereof, a derivative thereof " since no guidance is provided as to which of the myriad of polypeptide species encompassed by the claim will retain the characteristics of a CRD-$Leu_4Ile_{11}Cys_{13}$peptide 3(3-12)[MCP-1]. Since it is unpredictable which species of variant or derivative will have the characteristics of the CRD-$Leu_4Ile_{11}Cys_{13}$peptide 3(3-12)[MCP-1], the specification is not enabled for the full scope of using a variant or derivative of that species in a method of preventing or inhibiting an indication.

Applicant's arguments filed 6/9/2001 have been fully considered but they are not persuasive. Applicant argues that i) the specification provides guidance on how to identify peptides that fall within the scope of the claims, and that ii) the references cited by the Examiner are not applicable to the facts in the present case because they are not directed at a chemokine peptide, and iii) that it would not require undue experimentation to identify a variant of a chemokine peptide that falls within the scope of the claims.

The Examiner concedes that Applicant has provided the methods to identify peptides that fall within the scope of the claims. However, the Mikayama et al. and Voet et al. references cited in the previous office action demonstrated the unpredictability of the protein art as it relates to the effects of mutations on protein function. While not specifically directed towards mutants of chemokine peptides, the references are applicable because the unpredictability demonstrated in the references is applicable to mutations of any protein. Furthermore, given the unpredictability of the protein art, an analysis of the structural limitations given for the peptides ostensibly encompassed by the claim leads us to see that there are many possible peptides fitting into these limitations, i.e. 30 amino acids long, with 3 defined amino acid residues, to make and test all possible combinations with exactly 27 substitution changes would require many different combinations in accordance with the formula:

$$X^n \frac{(L)(L-1)(L-2)...[L-(n-1)]}{n!}$$ wherein, n = number of residues substituted, inserted, or deleted

L = length of polymer

x = number of different types of residues

so that we may calculate, given the limitations of exactly 27 substitutions in the 30 amino acid long polypeptide, would require:

$$27^{20}\frac{(30)(29)(28)(27)(26)...(4)}{27!} = 7.7 \times 10^{41}$$ different peptides to make and test

This analysis does not take into account all of the combinations with deletions. Applicant cites *In re Wands* to demonstrate that screening of biomolecules does not constitute undue experimentation. However, in the case of *Wands*, 143 hybridomas were obtained by fusion experiments, of which 9 were further characterized, four of which met the limitations of the claims (page 1405-1406). This is far different than the number of peptides species potentially encompassed by the claims in the instant case, as demonstrated above.

Based upon the evidence presented in the Mikayama et al. and Voet et al. references which demonstrates that the change of a single amino acid can radically alter protein function, the large number of peptides encompassed by the claims, and absent sufficient evidence to the contrary it would require undue experimentation for one of ordinary skill in the art to practice the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 17, 20-22, 34, 41-44, 52-56, 61-62 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 9520973.

WO 9520973 discloses peptides that bind the IL-1 receptor, and can inhibit binding of IL-1 to its receptor (page 1, lines 12-18). Examples of these peptides that are less than 30 amino acids in length and comprise the claimed WVQ sequence are shown on page 20 line 34 and line 37. An example of a peptide less than 30 amino acids in length that comprises the claimed KQK sequence is on page 25, line 7. WO 9520973 further discloses that the polypeptides can be administered to humans, and thus encompasses methods for therapeutic treatment of IL-1 related disorders that comprise administering a compound of the present invention in amounts sufficient to block or inhibit the binding of IL-1 to the IL-1R *in vivo* (page 38, lines 24-31). The indications to be treated with the compounds disclosed in WO 9520973 are disclosed in the instant application as being indications of chemokine-induced activity in the instant application (e.g. pro-inflammatory properties, fever and Kawasaki's disease, see pages 47 and 48 of the Specification and compare to page 38, line 34 to page 39, line 25 of WO 9520973). The peptides can be considered variants or derivatives of MCP-1, and CC or CXC chemokines, thus the claims are anticipated.

Conclusion

Claims 57-58 and 60 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 17, 20, 22, 34, 41-44, 52-56, 59, 61- 62 are rejected.

Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on 4/27/2001 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609(B)(2)(i). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
August 7, 2001

Prema Mertz
PREMA MERTZ
PRIMARY EXAMINER